



Food and Drug Administration  
10903 New Hampshire Avenue  
Document Control Center – WO66-G609  
Silver Spring, MD 20993-0002

Becton Dickinson and Company  
Gregory Payne, RAC  
Director of Regulatory Affairs  
10865 Road to the Cure, Suite 200  
San Diego CA 92121

June 8, 2015

Re: K151301  
Trade/Device Name: BD Veritor™ System for Rapid Detection of Flu A+B (Laboratory Kit)  
Regulation Number: 21 CFR 866.3330  
Regulation Name: Influenza Virus Serological Reagents  
Regulatory Class: I  
Product Code: GNX  
Dated: May 14, 2015  
Received: May 15, 2015

Dear Mr. Payne:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, “Misbranding by reference to premarket notification” (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH’s Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

Tamara V. Feldblyum -S<sup>for</sup>

Sally Hojvat, M.Sc., Ph.D.  
Director  
Division of Microbiology Devices  
Office of In Vitro Diagnostics  
and Radiological Health  
Center for Devices and Radiological Health

Enclosure

## Indications for Use

510(k) Number (if known)

K151301

Device Name

BD Veritor™ System for Rapid Detection of Flu A+B (Laboratory Kit)

### Indications for Use (Describe)

The BD Veritor™ System for Rapid Detection of Flu A+B is a rapid chromatographic immunoassay for the direct and qualitative detection of influenza A and B viral nucleoprotein antigens from nasopharyngeal wash, aspirate and swab in transport media samples from symptomatic patients. The BD Veritor System for Rapid Detection of Flu A+B is a differentiated test, such that influenza A viral antigens can be distinguished from influenza B viral antigens from a single processed sample using a single device. The test is to be used as an aid in the diagnosis of influenza A and B viral infections. A negative test is presumptive and it is recommended that these results be confirmed by viral culture or an FDA-cleared influenza A and B molecular assay. Outside the U.S. a negative test is presumptive and it is recommended that these results be confirmed by viral culture or a molecular assay cleared for diagnostic use in the country of use. FDA has not cleared this device outside the U.S. Negative test results do not preclude influenza viral infection and should not be used as the sole basis for treatment or other patient management decisions. The test is not intended to detect influenza C antigens.

Performance characteristics for influenza A and B nasopharyngeal (NP) washes/aspirates were established during January through March of 2011 when influenza viruses A/2009 H1N1, A/H3N2, B/Victoria lineage, and B/Yamagata lineage were the predominant influenza viruses in circulation according to the Morbidity and Mortality Weekly Report from the CDC entitled "Update: Influenza Activity—United States, 2010-2011 Season, and Composition of the 2011-2012 Influenza Vaccine." Performance characteristics may vary against other emerging influenza viruses.

Performance characteristics for influenza A and B NP swabs in transport media were established during January through April of 2012 when influenza viruses A/2009 H1N1, A/H3N2, B/Victoria lineage, and B/Yamagata lineage were the predominant influenza viruses in circulation according to the Morbidity and Mortality Weekly Report from the CDC entitled "Update: Influenza Activity—United States, 2011-2012 Season, and Composition of the 2012-2013 Influenza Vaccine." Performance characteristics may vary against other emerging influenza viruses.

If infection with a novel influenza virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to the state or local health department for testing. Virus culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Type of Use (Select one or both, as applicable)

☒ Prescription Use (Part 21 CFR 801 Subpart D)

☐ Over-The-Counter Use (21 CFR 801 Subpart C)

### CONTINUE ON A SEPARATE PAGE IF NEEDED.

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## 510(K) SUMMARY

**SUBMITTED BY:** BECTON, DICKINSON AND COMPANY  
10865 Road to the Cure, Suite 200  
San Diego, CA 92121  
Tel: (858) 795 7890  
Fax: (858) 795 7885

**CONTACT NAME:** Gregory P. Payne, RAC, Director Regulatory Affairs

**DATE PREPARED:** June 2, 2015, 2015

**DEVICE TRADE NAME:** BD Veritor™ System Flu A+B assay

**DEVICE COMMON NAME:** Influenza virus serological reagents

**DEVICE CLASSIFICATION:** 21 CFR 866.3330

**PREDICATE DEVICES :** BD Veritor™ System for Rapid Detection of Flu A+B Laboratory Kit  
(K120049,K121797,K132256,K132693,K133138)

**INTENDED USE :**  
Laboratory Kit

The **BD Veritor™** System for Rapid Detection of Flu A+B is a rapid chromatographic immunoassay for the direct and qualitative detection of influenza A and B viral nucleoprotein antigens from nasopharyngeal wash-aspirate and swab in transport media samples from symptomatic patients. The **BD Veritor** System for Rapid Detection of Flu A+B is a differentiated test, such that influenza A viral antigens can be distinguished from influenza B viral antigens from a single processed sample using a single device. The test is to be used as an aid in the diagnosis of influenza A and B viral infections. A negative test is presumptive and it is recommended that these results be confirmed by viral culture or an FDA-cleared influenza A and B molecular assay. Outside the U.S. a negative test is presumptive and it is recommended that these results be confirmed by viral culture or a molecular assay cleared for diagnostic use in the country of use. FDA has not cleared this device outside the U.S. Negative test results do not preclude influenza viral infection and should not be used as the sole basis for treatment or other patient management decisions. The test is not intended to

detect influenza C antigens. Performance characteristics for influenza A and B nasopharyngeal (NP) washes/aspirates were established during January through March of 2011 when influenza viruses A/2009 H1N1, A/H3N2, B/Victoria lineage, and B/Yamagata lineage were the predominant influenza viruses in circulation according to the *Morbidity and Mortality Weekly Report* from the CDC entitled "Update: Influenza Activity—United States, 2010-2011 Season, and Composition of the 2011-2012 Influenza Vaccine." Performance characteristics may vary against other emerging influenza viruses. Performance characteristics for influenza A and B NP swabs in transport media were established during January through April of 2012 when influenza viruses A/2009 H1N1, A/H3N2, B/Victoria lineage, and B/Yamagata lineage were the predominant influenza viruses in circulation according to the *Morbidity and Mortality Weekly Report* from the CDC entitled "Update: Influenza Activity—United States, 2011-2012 Season, and Composition of the 2012-2013 Influenza Vaccine." Performance characteristics may vary against other emerging influenza viruses. If infection with a novel influenza virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to the state or local health department for testing. Virus culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens

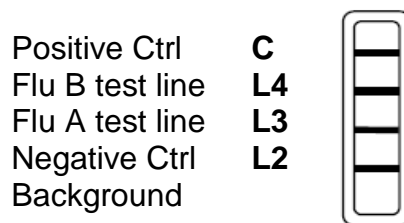
## **DEVICE DESCRIPTION :**

The BD Flu A+B test is a chromatographic assay to qualitatively detect influenza A and B viral antigens in respiratory specimens. The patient specimen is mixed in a prefilled unitized tube containing RV Reagent C and added to the test device. RV Reagent C contains mucolytic agents that function to break down mucus in a patient specimen thereby exposing viral antigens and enhancing detection in the assay device.

Processed specimens are expressed through a filter tip into a single sample well on the BD Flu A+B test device.

The specimen is mixed and added to the test device where influenza A or influenza B viral antigens bind to anti-influenza antibodies conjugated to detector particles on the BD Flu A+B test strip. The antigen-conjugate complex migrates across the test strip to the reaction area and is captured by an antibody line on the membrane. The assay utilizes a proprietary enhanced colloidal-gold particle at the test lines as the means for identifying the presence of influenza A or B viral antigens. The BD Flu A+B test devices are designed with five spatially-distinct zones including positive and negative control line positions, separate test line positions for the target analytes, and a background zone. The test lines for the target analytes are labeled on the test device as 'A' for Flu A position, and 'B' for Flu B position. The onboard positive control ensures the sample has flowed correctly and is indicated on the test device as 'C'. Two of the five distinct zones on the test device are not labeled. These two zones are an onboard negative control line and an assay background zone. The onboard negative control zone addresses non-specific signal generation and is not labeled on the test device. The remaining zone is used to measure the assay background and is also not labeled.

The BD Flu A+B assay incorporates an active negative control feature in each test to identify and compensate for sample-related, nonspecific signal generation. The BD Veritor™ System Reader uses a proprietary algorithm which subtracts nonspecific signal at the negative control line from the signal present at both the Flu A and Flu B test lines. If the resultant test line signal is above a pre-selected assay cutoff, the specimen is scored as positive. If the resultant test line signal is below the cutoff, the specimen is scored as negative. Use of the active negative control feature allows the BD Veritor™ System reader to correctly interpret test results that cannot be scored



visually because the human eye is unable to accurately perform the subtraction of the nonspecific signal.

### DEVICE COMPARISON:

The modified device differs from the currently marketed BD Veritor™ System Flu A+ B in the following way:

The labeling has been changed to reflect the addition of strain reactivity data for the following strains:

A/Fujian-Gulou/1896/2009	H1N1	B/Massachusetts/2/2012 (Yamagata Lineage)
A/Washington/24/2012	H1N1	B/Montana/5/2012
A/Switzerland//9715293/2013	H3N2	B/Phuket/3073/2013
A/Texas/50/2012	H3N2	B/Texas/06/2011 (Yamagata Lineage)
A/Anhui/01/05	H5N1	B/Wisconsin/01/2010 (Yamagata Lineage)
A/Vietnam/1203/04	H5N1	
A/Pheasant/New Jersey/1355/1998	H5N2	
A/Mallard/Netherlands/12/2000	H7N7	
A/Chicken/Hong Kong/G9/1997	H9N2	

### SUBSTANTIAL EQUIVALENCE:

The modified device BD Veritor™ System Flu A+ B is substantially equivalent to the current legally marketed device, BD Veritor™ System Flu A+B assay. Additions made to the labeling to add additional strain testing did not change the intended use of the device or the fundamental scientific technology.

A Risk Analysis was conducted and is detailed in the Design Control Summary Section. No new issues of safety and effectiveness were identified during this process.

Additions are as follows:

<b>Change</b>	<b>Potential Impact of Change</b>
<u>Addition of data for Strain reactivity of:</u> A/Fujian-Gulou/1896/2009 H1N1 A/Washington/24/2012 H1N1 A/Switzerland/9715293/2013 H3N2 A/Texas/50/2012 H3N2 A/Anhui/01/05 H5N1 A/Vietnam/1203/04 H5N1 A/Pheasant/New Jersey/1355/1998 H5N2 A/Mallard/Netherlands/12/2000 H7N7 A/Chicken/Hong Kong/G9/1997/H9N2 B/Massachusetts/2/2012 (Yamagata Lineage) B/Montana/5/2012 B/Phuket/3073/2013 B/Texas/06/2011 (Yamagata Lineage) B/Wisconsin/01/2010 (Yamagata Lineage)	Additional information provided to users regarding strain reactivity.



## 1. SUBMISSION STRATEGY

This premarket notification is submitted in accordance with the requirements of 21 CFR 807.81 as a Special 510(k): Device Modification for a device that has been cleared under the 510(k) process but has been modified using the design control requirements of the Quality Systems Regulations (QSR). Modifications made to the BD Veritor™ System Flu A+ B product insert did not change the intended use of the device or the fundamental scientific technology thereby meeting the requirements for submission of a Special 510(k).

This device submission is a modification of the currently marketed BD Veritor™ System Flu A+ B assay product insert to update the strain reactivity section of the product insert to include information on 14 new influenza strains.

## 2. DEVICE INFORMATION (CURRENT AND MODIFIED)

### LEGALLY MARKETED DEVICE (CURRENT)

Device Trade Name	BD Veritor™ System Flu A+ B assay
Common/Classification Name	Influenza virus serological reagents
Device Classification	21 CFR 866.3330 Class I
Product Code	GNX
Device Panel	Microbiology
Premarket Notification	K120049, K121797, K132256, K132693, K133138

### MODIFIED DEVICE

Device Trade Name	BD Veritor™ System Flu A+ B assay
Common/Classification Name	Influenza virus serological reagents
Device Classification	21 CFR 866.3330 Class I
Product Code	GNX
Device Panel	Microbiology

### 3. DEVICE DESCRIPTION

The BD Flu A+B test is a chromatographic assay to qualitatively detect influenza A and B viral antigens in samples processed from respiratory specimens. The processed specimen is added to the test device where influenza A or influenza B viral antigens bind to anti-influenza antibodies conjugated to detector particles on the A+B test strip. The antigen-conjugate complex migrates across the test strip to the reaction area and is captured by an antibody line on the membrane. Results are interpreted by the BD Veritor™ System Reader, a portable electronic device which uses a reflectance-based measurement method to evaluate the line signal intensities on the assay test strip, and applies specific algorithms to determine the presence or absence of any target analyte(s). A liquid crystal display (LCD) on the instrument communicates the results to the operator.

### 4. PRINCIPLE OF PROCEDURE

The BD Flu A+B test is a chromatographic assay to qualitatively detect influenza A and B viral antigens in respiratory specimens. The patient specimen is mixed in a prefilled unitized tube containing RV Reagent C and added to the test device. RV Reagent C contains mucolytic agents that function to break down mucus in a patient specimen thereby exposing viral antigens and enhancing detection in the assay device. Processed specimens are expressed through a filter tip into a single sample well on the BD Flu A+B test device.

The specimen is mixed and added to the test device where influenza A or influenza B viral antigens bind to anti-influenza antibodies conjugated to detector particles on the BD Flu A+B test strip. The antigen-conjugate complex migrates across the test strip to the reaction area and is captured by an antibody line on the membrane. The assay utilizes a proprietary enhanced colloidal-gold particle at the test lines as the means for identifying the presence of influenza A or B viral antigens.

The BD Flu A+B test devices are designed with five spatially-distinct zones including positive and negative control line positions, separate test line positions for the target analytes, and a background zone. The test lines for the target analytes are labeled on the test device as 'A' for Flu A position, and 'B' for Flu B position. The onboard positive control ensures the sample has flowed correctly and is indicated on the test device as 'C'. Two of the five distinct zones on the test device are not labeled. These two zones are an onboard negative control line and an assay background zone. The onboard negative control zone addresses non-specific signal generation and is not labeled on the test device. The remaining zone is used to measure the assay background and is also not labeled.

Positive Ctrl	<b>C</b>
Flu B test line	<b>L4</b>
Flu A test line	<b>L3</b>
Negative Ctrl	<b>L2</b>
Background	



The BD Flu A+B assay incorporates an active negative control feature in each test to identify and compensate for sample-related, nonspecific signal generation. The BD Veritor™ System Reader uses a proprietary algorithm which subtracts nonspecific signal at the negative control line from the signal present at both the Flu A and Flu B test lines. If the resultant test line signal is above a pre-selected assay cutoff, the specimen is scored as positive. If the resultant test line signal is below the cutoff, the specimen is scored as negative. Use of the active negative control feature allows the BD Veritor™ System reader to correctly interpret test results that cannot be scored visually because the human eye is unable to accurately perform the subtraction of the nonspecific signal.

The BD Veritor™ System Reader measures the amount of light reflected from various zones along the assay strip. The measurement of the assay background zone is an important factor during test interpretation as the reflectance is compared to that of the control and test zones. A background area that is white to light pink indicates the device has performed correctly. The instrument analyzes the reflectance data to provide the proper interpretation.

## **5. DEVICE COMPARISON**

The BD Veritor™ System Flu A+ B assay is substantially equivalent to the current legally marketed device, BD Veritor™ System Flu A+ B assay. Modifications made to the BD Veritor™ System Flu A+ B assay product insert did not change the intended use of the device or the fundamental scientific technology.

The BD Veritor™ System Flu A+ B assay product insert differs from the current legally marketed BD Veritor™ System Flu A+ B assay product insert in the following way:

The product inserts includes an update to include information on Strain Reactivity to 14 additional strains of flu virus.

## **6. DESIGN CONTROL SUMMARY**

Our Risk Assessment process is based on a BD Product Risk Management procedure which meets the requirement for risk management as set forth in ISO 14971:2007 and EN ISO 14971:2012. Using this procedure, the following are estimated:

- the Hazard,
- the Adverse Effect (Harm to Patient),
- the Potential Causes of the Hazard,
- The probability of Severity and
- The probability of Occurrence are estimated.

Based on a resulting calculated Risk Index, Risk Control Measures are identified, required verification and validation activities are determined, and verification of the effectiveness of risk control measures is determined.

The tables below are taken from the procedure and provide guidelines to determine the probability of severity and occurrence. Additionally, a risk chart is provided below which depicts the areas of risk.

Indicator	Category	Definition
S-1	Negligible	No adverse health consequences; may result in annoyance to user or to patient. Could include cosmetic defect and/or need to replace defective product prior to initial use.
S-2	Limited	<p>Injury, without a significant discomfort or any degree of disability. Symptoms are transient easily tolerated with no interference with subject's daily activities. Illness or injuries are transient, self-limited and require no medical intervention or require medical intervention that is limited in scope (i.e., non-significant risk).</p> <p><u>Device Examples:</u> product failure requiring: reinsertion of a peripheral IV catheter, repeat skin injection (without impact to dose), peripheral venous blood sampling, or one which results in clean (unused on patient, not contaminated) needle stick and/or blade injury, or which results in a mild, non-painful electrical shock, first degree (superficial) burns, or mild retinal laser light exposures.</p> <p><u>IVD Examples:</u>  <i>Patient:</i> erroneous patient results (e.g. false positive results, false negative results, incorrect patient ID with results), delayed treatment for IVD medical devices which are not the sole determinant and are classified in lower risk classes. Although the erroneous patient results might not be corrected by other means, the impact to the patient is negligible to none.  <i>Third party (e.g. user, service engineer, etc.):</i> non painful electrical shock, first degree (superficial) burns, mild retinal laser light exposure.</p>
S-3	Moderate	<p>Injury which may include significant discomfort, minor non-permanent injury and/or temporary disability. Symptoms are temporary and /or reversible. These injuries usually require medical intervention to treat the injury. This category includes, but is not limited to:</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Injuries which require the need for minor, local surgery or the need to repeat a semi-invasive low-risk procedure due to product failure.</li> <li><input type="checkbox"/> The misdiagnosis or wrong treatment of a non-serious illness due to erroneous results</li> </ul> <p><u>Device Examples:</u> product failures resulting in fractured needle requiring local exploratory surgery to remove part, requiring reinsertion of a central venous catheter, peripherally inserted central catheter, or invasive diagnostic procedure such as a spinal tap, or which results in a contaminated sharps injury without seroconversion or transmission of blood borne disease, or which results in painful electrical shock, second degree (partial thickness) burns or moderate retinal laser light exposure.</p> <p><u>IVD Examples:</u>  <i>Patient:</i> erroneous patient results (e.g. false positive results, false negative results, incorrect patient ID with results), delayed treatment for IVD medical devices which are not the sole determinant but which are classified in higher risk classes.  <i>Third party (e.g. user, service engineer, etc.):</i> painful electrical shock, second degree burns, moderate retinal laser light exposure, contaminated sharps injury without seroconversion or transmission of blood borne disease.</p>

S-4	Severe	<p>Injury which results in severe symptoms, significant injury, potential long-term risk to health, or permanent impairment as a direct result of product failure, or due to a delay in treatment as a result of product failure. The injury/symptoms may be irreversible despite medical intervention, but are not immediately life threatening. This category includes, but is not limited to:</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Injuries which require major or invasive (i.e., moderate to high-risk) surgery or other intervention for treatment, exposure of patient to a high level of cumulative risk due to multiple medical interventions, or injuries which require patient hospitalization or which extend length of patient hospitalization for treatment.</li> <li><input type="checkbox"/> The transmission or causation of a potentially chronically debilitating or life threatening disease as a result of the product malfunction</li> <li><input type="checkbox"/> The misdiagnosis or wrong treatment of a serious illness due to erroneous results</li> </ul> <p>Device Examples: product failures that require such procedures as exploratory laparotomy or other invasive diagnostic procedure with significant risk, removal and reinsertion of a fully inserted pulmonary arterial catheter, or retrieval of catheter fragment from the heart. Also included are product failures which result in loss of sight, amputation or loss of use of a limb, pneumonia, bacteremia, seroconversion for blood borne disease such as HIV/AIDS or Hepatitis C, electrical exposure above the “let go” threshold but which does not result in cardiac or respiratory compromise, widespread partial thickness or limited full-thickness (third degree) burns or severe moderate retinal laser light exposure.</p> <p>IVD Examples:  Patient : erroneous patient results (e.g. false positive results, false negative results, incorrect patient ID with results), delayed treatment for IVD medical devices which are the sole determinant and/or are in the highest risk class  Third party (e.g. user, service engineer, etc.): electrical exposure above the “let go” threshold but which does not result in cardiac or respiratory compromise, third degree burns, severe retinal laser light exposure, contaminated sharps injury with seroconversion for blood borne disease such as HIV/AIDS or Hepatitis C.</p>
S-5	Catastrophic	<p>Fatal or immediately life threatening. Fatal means death has already occurred. Life threatening means that death could occur in the near term despite treatment or that the patient was or would be at immediate risk of death if medical intervention had not occurred</p> <p>Device Examples: anaphylactic reaction, severe hemorrhage, cardiac tamponade, cardiac arrest, septic shock, electrocution with cardiac or respiratory compromise, extensive third-degree burns.</p> <p>IVD Examples:  Patient: erroneous patient results (e.g. false positive results, false negative results, incorrect patient ID with results) for IVD medical devices with a large public health risk (e.g. contamination of the blood supply).  Third party (e.g. user, service engineer, etc.): electrocution with cardiac or respiratory compromise, extensive third-degree burns.</p>

Probability Indicator	Category	Probability of Harm (Definition)
P1	Improbable	Extremely unlikely in the life of the system at any given site
P2	Remote	Likely to occur once in the life of the system at any given site
P3	Occasional	Likely to occur once every year for each system at any given site
P4	Reasonably Probable	Likely to occur a few times per year for each system at any given site
P5	Frequent	Likely to occur many times per year for each system at any given site

Three-Region Risk Chart						
		Severity				
		S1	S2	S3	S4	S5
Occurrence	P5	GR	RE	RE	RE	RE
	P4	GR	YE	RE	RE	RE
	P3	GR	GR	YE	RE	RE
	P2	GR	GR	GR	YE	RE
	P1	GR	GR	GR	YE	YE

Risk regions include:

**Insignificant (GR)** – individual risks in the green region are deemed negligible in comparison with other risks and in relation to the benefit of using the product. Even if the risk falls into this region, the risk must be reduced as far as possible. For risks falling into this region, the medical benefit are considered to outweigh the individual residual risk since the combination of the occurrence and severity is considered low. These risks do not require individual risk benefit analysis. Because risk of harm in this region are deemed negligible, risk control measures implemented in this region, will not require documented verification of risk control measure effectiveness.

**Investigate (YE)** – individual risks in the yellow region are not negligible in comparison with other risks, therefore further risk reduction must be investigated. This category requires evaluation for risk reduction and once all possible risk control measures have been implemented, the residual risk is not reduced to insignificant (GR) is not possible, the individual item in this region require a documented risk/benefit analysis to document acceptance of the residual risk (See Attachment 3 for a Risk Benefit Analysis model).

**Unacceptable/Intolerable (RE)** - individual risks in the red region are unacceptable. This region requires the implementation of risk control measures to reduce the risk. In general, BDDS products should not have items with residual risks falling into this region. However, in an exceptional and rare circumstance, these items may be

documented in the risk/benefit analysis with approval by Medical Affairs at a director level or higher.

The risk assessment identified the need to confirm the Veritor system's reactivity to new strains forecast for 2015/2016 Influenza Season, as well as other strains not previously tested available through CDC and WHO.

### RESULTS OF THE ANALYSIS:

The results of the analysis indicated an initial possible combination of severity and occurrence that fell into S-3/P-3 category. To implement the indicated investigation, Protocol SDSP15001 was developed and approved based on previously accepted FDA submissions regarding strain reactivity. The design of the study is below and is replicated from a previous Special 510(k) submission. Acceptability criteria was the ability of the BD Veritor test to detect these additional Flu strains. Veritor was successful in detecting all strains tested. The data to be included in the insert are the actual values obtained during this testing. The results of the strain testing reduced the probability of occurrence from P-3 to P-1 and reduced the risk to the "negligible" category.

<b>Hazard</b>	False Negative		<b>Risk Control Measure</b>	<b>Testing</b>
<b>Adverse Effect (Harm)</b>	Effect on patient is that they could be inappropriately treated leading to flu progression			Obtain and test additional flu strains
<b>Probability of Severity</b>	S-3			<b>Labeling</b>
<b>Potential Causes of the Hazard</b>	Assay does not detect the predicted strains for 2015/2016 Flu Season or other available new and circulating strains			Update PI with new reactivity after FDA special 510(k) clearance
<b>Probability of Occurrence</b>	P-3		<b>Risk Control Measure Effectiveness Reference</b>	SDSP15001
<b>Existing Risk Control Measure</b>	Current strain reactivity has been determined and is provided in the Product Insert		<b>Probability of Severity</b>	S-3
<b>Risk Index</b>	YE		<b>Probability of Occurrence</b>	P-1
<b>Responsibility for Risk Control Measure</b>	R&D		<b>Risk Index</b>	GR

Finally, after review and clearance of this submission by FDA, a change control will be initiated to document this activity in the design history file and to route the new PI for approval.

Modifications to the product insert will be implemented in accordance to BD Change Control Procedure RDQP0401.

## 7. SUMMARY OF STUDIES

Study acceptance criteria were that the Veritor Flu A+B assay system needed to give a positive instrumented read with samples of subject flu viruses in order to support this claim in a revised Package Insert. Subject Flu strains were chosen based on strains forecasted for the 2015/2016 Flu season, additional influenza strains available from CDC and WHO and also in response to customer requests. The testing protocol was the same as has been used in previous submissions to FDA regarding strain reactivity and is detailed in BD protocol Document SDSP15001. This study was conducted under the direction of Richard Anderson Ph.D. at the R/D laboratories in San Diego, CA. Viral material in allantoic fluid from chicken eggs was used in this study.

### Viruses tested

Twelve virus strains were provided by the WHO Collaborating Centre for Surveillance, Epidemiology and Control of Influenza and the US Centres for Disease Control. The two strains provided by National Institute for Biological Standards and Control (UK) used in this testing, A/Switzerland//9715293/2013 and B/Phuket/3073/2013, were received as lyophilized preparations and were subsequently reconstituted, amplified in culture and titred following procedures outlined in the WHO Manual on Animal Influenza Diagnosis and Surveillance (2002) before supplying this material for reactivity testing in the Veritor system.

### Materials and procedures for this step are as follows:

MDCK cells:	ATCC, Cat# CCL-34
TPCK-trypsin (2 mg/ml):	Sigma, Cat #T1426-50MG
Complete MEM medium for MDCK cells:	ATCC, Cat # 30-2003
Penicillin (10,000 U/ml) + Streptomycin (10,000 µg/ml)	Invitrogen, Cat # 15140-122
Fetal Bovine Serum	Sigma Cat. # 30-2020
DMSO	Sigma Cat #D2438

1. Prepare TPCK-trypsin stocks:
  - a. Dissolve 20 mg TPCK-trypsin in 10 mL dH<sub>2</sub>O. Filter through 0.2 µL membrane. Store in aliquots at -20°C
2. Prepare Complete MEM medium (CMM):
  - a. 500 mL MEM + 5.5 mL Penicillin (10,000 U/mL)/ Streptomycin (10,000 µg/mL)
3. Prepare cell growth medium (CGM) from CMM above: 500mL CMM + 50mL FBS
4. Prepare compete virus growth medium (VGM) : 0.5 mL of TPCK-trypsin to CMM.
5. Freeze Medium: Add 5% DMSO to cell growth medium, freeze overnight at minus 80°C in liquid Nitrogen.

MDCK cells are routinely maintained in T-75 flasks in Cell Growth Media (CGM) supplemented with 10 % (v/v) FBS and Penicillin/Streptomycin. One day before virus infection, MDCK cells were seeded into T-25 and T-75 flasks at 50-60%



confluency resulting in 90-100% confluency at the time of infection. Reconstituted virus was incubated with CGM and VGM at 37°C, in a 5% CO<sub>2</sub> incubator for 1 hour. The flasks containing MDCK cells were washed with VGM and 1 ml of the incubated virus was added to a T-25 flask and the remaining to a T-75 flask, and then incubated at 37°C, 5% CO<sub>2</sub> incubator for 2 hours. These flasks were washed twice with VGM, and then 3 mL of VGM was added to the T-25 flask, 10 mL of VGM was added to the T-75 flask. The infected cells were incubated at 37°C, in a 5% CO<sub>2</sub> incubator for 2-5 days. The flasks were examined under a microscope for signs of infection. When more than 80% cells were infected, the supernatants were aliquoted into 1 mL tubes and kept in liquid nitrogen. These preparations were assigned a lot number based on date.

Viral titer was measured using a 96 well plate with MDCK host cells inoculated with 10 fold serial dilutions of virus. After 3-4 days at 37°C in a CO<sub>2</sub> incubator, the titration plate was examined for Viral Cytopathic effects and TCID<sub>50</sub> is calculated by the Reed-Muench formula

No.	Sample Description	Lot No.	Titer of stock
1	A/Fujian-Gulou/1896/2009 H1N1	59433572	1.8 x 10 <sup>9</sup> CEID <sub>50</sub> /mL
2	A/Washington/24/2012 H1N1	7/12/2013	3.16 x 10 <sup>8</sup> EID <sub>50</sub> /mL
3	A/Switzerland//9715293/2013 H3N2	02262015	1.3 x 10 <sup>6</sup> TCID <sub>50</sub> /mL
4	A/Texas/50/2012 H3N2	61757568	3.5 x 10 <sup>6</sup> TCID <sub>50</sub> /mL
5	A/Anhui/01/05 H5N1	62539790	512 HA
6	A/Vietnam/1203/04 H5N1	59613801	512 HA
7	A/Pheasant/New Jersey/1355/1998 H5N2	61647886	256 HA
8	A/Mallard/Netherlands/12/2000 H7N7	61572488	512 HA
9	A/Chicken/Hong Kong/G9/1997 H9N2	60429654	1024 HA
10	B/Massachusetts/2/2012 (Yamagata Lineage)	61649126	1.0 x 10 <sup>10</sup> CEID <sub>50</sub> /mL
11	B/Montana/5/2012	7/12/2013	2.51 x 10 <sup>8</sup> EID <sub>50</sub> /mL
12	B/Phuket/3073/2013	04102015	2.43x10 <sup>7</sup> TCID <sub>50</sub> /mL
13	B/Texas/06/2011 (Yamagata Lineage)	61070013	6.2 x 10 <sup>8</sup> CEID <sub>50</sub> /mL
14	B/Wisconsin/01/2010 (Yamagata Lineage)	61176817	2.8 x 10 <sup>6</sup> CEID <sub>50</sub> /mL

10 fold dilutions from the stock received were tested in triplicate using the BD Veritor System Flu A+B test to establish the approximate level for the LOD.

## BD Veritor System Flu A+B test materials

Veritor System Flu A+B devices: two lots  
 expiration date 2017/07/24  
 expiration date 2015/10/13  
 Reagent C, lot# 11071104, #13092703  
 Unitized tube, lot# IM046-0000  
 Test Standard diluent lot #90-185  
 Veritor System Readers SN #1212145789CN2

## Conclusions

Nine Flu A strains and Five Flu B strains were enrolled in this study. The data indicate that all Flu A strains enrolled in this study can be detected by the Flu A line of the Veritor System Flu A+B device and none cross react with the Flu B line. All five Flu B strains enrolled in this study can be detected by the Flu B line of the Veritor System Flu A+B device and none cross react with the Flu A line. The lowest concentration (LOD) of influenza A and influenza B viruses that can be detected by Veritor System Flu A+B device are listed here:

No.	Strain	Final Dilution Factor	Estimated LOD <sup>1</sup>
1	A/Fujian-Gulou/1896/2009 H1N1	4000	$4.5 \times 10^5$ CEID <sub>50</sub> /mL
2	A/Washington/24/2012 H1N1	10000	$3.16 \times 10^4$ EID <sub>50</sub> /mL
3	A/Switzerland//9715293/2013 H3N2	4000	$3.25 \times 10^2$ TCID <sub>50</sub> /mL
4	A/Texas/50/2012 H3N2	2000	$1.75 \times 10^3$ TCID <sub>50</sub> /mL
5	A/Anhui/01/05 H5N1	2000	0.512 HA
6	A/Vietnam/1203/04 H5N1	2000	0.512 HA
7	A/Pheasant/New Jersey/1355/1998 H5N2	1000	0.256 HA
8	A/Mallard/Netherlands/12/2000 H7N7	2000	0.256 HA
9	A/Chicken/Hong Kong/G9/1997 H9N2	1000	1.024 HA
10	B/Massachusetts/2/2012 (Yamagata Lineage)	8000	$1.25 \times 10^6$ CEID <sub>50</sub> /mL
11	B/Montana/5/2012	800	$3.14 \times 10^5$ EID <sub>50</sub> /mL
12	B/Phuket/3073/2013	4000	$6.08 \times 10^3$ TCID <sub>50</sub> /mL
13	B/Texas/06/2011 (Yamagata Lineage)	1000	$6.2 \times 10^5$ CEID <sub>50</sub> /mL
14	B/Wisconsin/01/2010 (Yamagata Lineage)	4000	$7.0 \times 10^2$ CEID <sub>50</sub> /mL

<sup>1</sup> Estimated LOD is the lowest concentration of influenza A and B virus strains that can be detected by the BD Veritor System Flu A + B Assay in 3/3 replicates.

The strain reactivity data provided above and proposed for inclusion into the PI demonstrates that the acceptance criteria were met by all strains tested.

## **8. DECLARATION OF CONFORMITY**

The manufacturing facility is in conformance with design control procedure requirements as specified in 21 CFR 820.30. This statement can be found in Appendix 1.

## **9 . CONCLUSION FROM THE TESTING**

The studies conducted on the BD Veritor™ System Flu A+B assay demonstrated that labeling changes can be made to the product insert to reflect the analytical sensitivity and reactivity data generated. This will be used to update the strain reactivity section of the product insert to include information on the aforementioned strains.

## **10. LABELING**

Copies of the revised product inserts for the BD Veritor System Flu A+B assay are provided in Attachment 3. The labeling for this device has been modified from the current labeling to update the strain reactivity section of the product insert. The changes can be found in Appendix 3 page 10.

The intended use of this modified device as described in the labeling has not changed as a result of this modification.

All performance characteristics as well as other sections of the Package Insert from the current BD Veritor System Flu A+B assay have remained the same in the revised Package Insert.